REMARKS

Claims 1-4 and 150-209 presently appear in this case. Claims 150, 151, 156, 157, 162, 163, 167 and 168 have been rejected. Claims 1-4 have been allowed. Claims 152-155, 158-161, 164-167, and 170-172 have been objected to for depending from a rejected claim, but presumably are otherwise allowable. The official action of September 17, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

I Statements under 37 C.F.R. §1.173(c)

The following statements are made pursuant to the requirements of 37 C.F.R. §1.173(c). Patent claims 1-4 are pending and have not been changed from the language of these claims as they appeared in the patent. Added claims 5-149 have been cancelled. Claims 150-209 are also pending.

Claims 150, 156, 162 and 168 have been amended to specify that the pharmaceutical formulation is in unit dosage form. The concept of unit dosage form is implicitly and inherently supported by the disclosure at column 9, lines 22-32, of the present specification, which speaks of the presentation of the monoclonal antibody "as a pharmaceutical formulation," in which pharmaceutically acceptable carriers and optionally other therapeutic ingredients are also present. The language of the amended claims complies with the written

description requirement of 35 U.S.C. § 112, as the concept of a pharmaceutical formulation for therapeutic administration must necessarily and implicitly support that such formulation will be in unit dosage form.

The inventor's explicit disclosure of the monoclonal antibody in a pharmaceutical formulation for therapeutic administration must comprehend the concept that the formulation will be in unit dosage form. Attached to applicant's amendment of August 9, 2004, was a printout from the internet showing that the "Dictionary Barn" Medical Dictionary defines "formulation" as:

> <pharmacology> The mixture or prescribed recipe for packaging a protein pharmaceutical, the process of developing such a formulation.

Thus, the term "formulation" includes the concept of "packaging", which would require that the protein pharmaceutical be packaged in unit dosage form.

Further in this regard, the examiner's attention is invited to the Guidelines for the Examination of Patent Applications under 35 U.S.C. § 112, Para. 1, "Written Description" Requirement, appearing at §2163 of the May 2004 edition of the Manual of Patent Examining Procedure. On page 2100-167, in discussing new or amended claims, the MPEP states:

> While there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure.

See also page 2100-175, relating to amended claims or claims asserting entitlement to the benefit of an earlier priority date, where it states:

> To comply with the written description requirement of 35 U.S.C. § 112, para. 1, ... each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure. When an explicit limitation in the claim "is not present in the written description whose benefit is sought, it must be shown that a person of ordinary skill would have understood, at the time the patent application was filed, that the description requires that limitation." *Hyatt v Boone*, 146 F.3d 1348, 1353, 47 USPQ2d 1128, 1131, (Fed. Cir. 1998).

The same statement is repeated in MPEP 2163.05. A person of ordinary skill reading the disclosure about putting the antibody and a pharmaceutically acceptable carrier into a "pharmaceutical formulation" for therapeutic administration, would have understood that the description requires the unit dosage form limitation. Accordingly, this term is sufficiently supported by the present disclosure to comply with the written description requirement of the first paragraph of 35 U.S.C. §112.

Claim 173 is newly presented by the present paper. Claim 173 is identical to previously appearing claim 167,

except that paragraph (A)(i) (in claim 168, from which claim 173 ultimately depends) provides that the antibody "is obtainable using residues 1-28 of β-amyloid as an immunogen." This language tracks the language of section (A)(i) of previously appearing claims 155 and 161 (insofar as they ultimately depend from independent claims 150 and 156).

Reference is made to the claim support chart accompanying applicant's amendment of February 23, 2004, which includes a section specifically relating to support for this subparagraph of claims 150 and 156. Support for claim 173 is the same as that presented in said claim support chart with respect to claim 167.

Claim 173 was intended to have been submitted with claims 168-172 in applicant's supplemental amendment of August 18, 2004, but was inadvertently omitted.

Claims 174-209 are simply allowable claims 152-155, 158-161, 164-167 and 170-173, rewritten into independent claim form. Claim 174, for example, is identical to previously appearing claim 150, combined with the subject matter of previously dependent claims 151-153. Thus, the subject matter of allowable claims 152 and 153 have been combined as alternatives in paragraph (A) of claim 174. Claim 175 is the same as previously appearing claim 152, claim 176 is identical to previously appearing claim 153, and claim 177 is identical

to previously appearing claim 154. Claim 178 is previously appearing claim 155/150 rewritten in independent form. Claims 179-182 are the same as previously appearing claims 151-154, but dependent upon allowable claim 178. Thus, these claims are effectively identical to previously appearing claims 155/151, 155/152, 155/153 and 155/154. Accordingly, new claims 178-182 cumulatively have the same scope as previously appearing multiply dependent claim 155. Similarly, claims 183-191 are the same as claims 158-161 rewritten in independent form in the same manner as discussed above for claims 174-182, claims 192-200 are the same as allowable claims 164-167 rewritten in independent form, and claims 201-209 are the same as claims 170-173 rewritten in independent form. We assume that claim 173, if it had been earlier submitted, would also have been indicated to be allowable for the same reasons that claims 155, 161, 167, and 170-172 were indicated to be allowable.

As no new limitations were added to new claims 174-209 that were not in previously appearing claims 152-155, 158-161, 164-167 and 170-173, support for all of these recitations of the claims can be found in the claim support chart accompanying applicant's amendment of February 23, 2004.

II **Brief Summary of the Invention**

Briefly, the present invention relates to pharmaceutical formulations comprising an antibody or an antigen binding fragment thereof and a pharmaceutically acceptable carrier. The antibody and fragment recognize an epitope within residues 1-28 of β-amyloid or are obtainable using residues 1-28 of β-amyloid as an immunogen and they inhibit aggregation of β-amyloid or they maintain the solubility of soluble β-amyloid. The formulation is preferably in unit dosage form. The antibody is preferably a monoclonal antibody, and more preferably a human monoclonal antibody, a genetically engineered monoclonal antibody, or a single chain antibody. The β-amyloid is preferably human β-amyloid.

III **Statement under 37 C.F.R. §1.178(b)**

The present patent is not and has not been involved in any prior or concurrent proceeding, including interferences, reissues, reexaminations and litigation.

IV **Supplemental Declaration under 37 C.F.R. §1.175(b)(1)**

In view of the present amendment to the claims, another supplemental reissue declaration is in preparation and will be filed soon to comply with 37 C.F.R. §1.175(b)(1).

V Information Disclosure Statement

Attached hereto is an Information Disclosure Statement including European patent publication 557,270. This European patent corresponds to US patent 5,004,697, which has previously been submitted in an Information Disclosure Statement, and is presently of record in this case.

VI Anticipation Rejection over Bickel

Claims 150, 151, 156, 157, 162, 163, 168 and 169 have been rejected under 35 U.S.C. §102(a) as being anticipated by Bickel. The examiner pointed out that applicant previously traversed this rejection on the grounds that (a) the claims required the antibody to be in a "pharmaceutical formulation" and (b) that Bickel uses a Tris solution, which is not a "pharmaceutically acceptable carrier". The examiner did not accept applicant's traversal on ground (a), as the examiner found "pharmaceutical formulation" to be a mere intended use and not a claim limitation. The examiner did not accept ground (b), citing a reference allegedly teaching that use of a buffered Tris solution at pH=7.4 is not inconsistent with use as a pharmaceutical. This rejection is respectfully traversed.

The claims have now been amended to specify in the body of the claim that the formulation comprises a "unit dosage" of the specified components. This term is not merely

a statement of intended use, but is a physical form that is inextricably related to the therapeutic utility. The antibodies of Bickel have no therapeutic utility. Therefore, the claims are not anticipated by Bickel.

The recitation of "unit dosage" is not new matter for the reasons discussed above in the section I. This merely makes explicit in the body of the claim that which had been implied by the term "pharmaceutical formulation" in the preamble. While it is not believed that the examiner's citation of *In re Ngai*, 70 USPQ2d 1862 (Fed. Cir. 2004) is applicable, as the previous arguments had nothing whatsoever to do with printed matter, it is clearly inapplicable to the claims as presently amended, because the unit dosage feature is in the body of the claim and is a physical limitation not disclosed by Bickel, and not related to printed matter. Clearly this limitation distinguishes the present invention from Bickel.

Applicant hereby withdraws its argument that Tris is not pharmaceutically acceptable. Applicant is now aware that Tris buffer is also known under the name tromethamine, and under this name, it is listed on the FDA's GRAS list. Nevertheless, the present claims are not anticipated by Bickel because of the "unit dosage" requirement, as discussed above.

Accordingly, reconsideration and withdrawal of this rejection is respectfully urged.

VII **Anticipation Rejection over Stern**

Claims 150, 151, 156, 157, 162, 163, 168 and 169 have been rejected under 35 U.S.C. §102(b) as being anticipated by Stern. The examiner points out that applicant had previously traversed this rejection on the grounds that (a) Stern does not teach or make obvious a pharmaceutical formulation nor use of AMY-33 antibody as a therapeutic and (b) the commercially available solution of AMY-33 from SIGMA contains sodium azide. The examiner did not accept the arguments on ground (a) for the same reasons as discussed hereinabove for Bickel and did not accept the arguments on ground (b), as there is no disclosure that Stern purchased the antibodies from SIGMA, and because one would not leave an azide in an antibody, even for nontherapeutic purposes. This rejection is respectfully traversed.

As discussed hereinabove with respect to Bickel, the claims have now been amended to specify unit dosage form. Accordingly, the examiner's reasons why applicant's previous ground (a) arguments were not acceptable are no longer available. As discussed above, the claims have a positive limitation of unit dosage form that is not disclosed by Stern.

Accordingly, this rejection should be withdrawn for the same reasons as discussed above with respect to Bickel.

Furthermore, the examiner appears to have overlooked the third ground asserted by applicant why the Stern reference does not anticipate. Stern does not use its antibody preparation as a therapeutic, and takes no steps to ensure that the composition would be pharmaceutically acceptable. Indeed, it is apparent that Stern used the entire monoclonal antibody supernatant in making his ELISA solution. See page 974 under the heading "Immunohistochemistry", referring to "MAb supernatants". MAb supernatants will include all kinds of proteins made by the hybridoma besides the antibody in question. In view of the fact that there was apparently no attempt to purify the antibody from these accompanying proteins, the resulting ELISA solution cannot be said to be a pharmaceutical formulation comprising an antibody in a pharmaceutically acceptable carrier.

Accordingly, for both of these reasons, reconsideration and withdrawal of this rejection are believed to be in order.

VIII **Objection to Claims 152-155, 158-161, 164-167 and 170-172**

It is noted that claims 152-155, 158-161, 164-167 and 170-172 have been objected to for depending from rejected claims. Apparently, these claims would be in condition for

allowance if rewritten in independent form with all of the limitations of the claims from which they depend.

New claims 174-209 are now being submitted, which are effectively claims 152-155, 158-161, 164-167 and 170-173 rewritten into independent form. We have assumed that claim 173, if it had been earlier submitted, would also have been indicated to be allowable for the same reasons that claims 155, 161, 167 and 170-172 were indicated to be allowable. Thus, at least claims 174-209 should now be allowed.

IX Conclusion

It is submitted that all of the claims now present in the case clearly define over the references of record, and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office, on the date shown below.

Jonathan Brammer
Name

Signature

March 17, 2005
Date